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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 06/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/441,055	USUDA ET AL.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-33 and 35* is/are pending in the application.

4a) Of the above claim(s) *1-9 and 11-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on 05/09/2005 has been entered.

2. Claims 31-33 and 35 are under consideration in this Office Action.

3. The rejection of claims 31-33 and 35 under 35 USC 101 as being directed to non-statutory subject matter has been withdrawn in view of applicants' amendments to the claims.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

4.. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 31, 33, and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31 and 33 are vague and indefinite for reciting "enhanced" activity of any homoserine transsucinylase and cystathionine γ-synthase. The metes and bounds of the claim are unclear since there is no point of reference for any "enhanced" activity. Claim 35 which depends from claim 31 is also rejected because it does not correct the defect of claim 31.

Amending the claims to recite the activity of homoserine transsucinylase and cystathionine γ-synthase in the recited recombinant *Escherichia* bacterium is increased compared to an unmodified *Escherichia* bacterium may overcome the rejection.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

6. Claims 31-33 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 05/09/2005 have been considered but they are not persuasive. Applicants' position is that the scope of the recited *metA*, *metK*, *metB*, and *metL* genes are limited to an *Escherichia* bacterium and that the specification provides extensive lists of references from which the nucleotide sequences of the endogenous *Escherichia metA*, *metK*, *metB*, and *metL* genes may be found. The Examiner respectfully disagrees for reasons of record as supplemented below.

According to MPEP §2111, claims must be given their broadest reasonable interpretation consistent with the specification and that such interpretation of the claims must also be consistent with the interpretation that those skilled in the art would reach. The claims of the instant invention must be read in light of the specification to thereby interpret limitations explicitly recited in the claims. Thus, limitations of the specification cannot be read into the claims to narrow the scope of the claims by implicitly adding disclosed limitations which are not recited in the claims.

The claims as amended are not specifically limited to the endogenous *Escherichia metA, metK, metB, and metL* genes since the claims do not recite that the claimed genes are endogenous to the recited recombinant *Escherichia* bacterium. Furthermore, in view of MPEP §2111 the list of references cited in the specification for the specific nucleotide sequences of the recited *metA, metK, metB, and metL* genes are limitations from the specification that cannot be read into the claims to narrow the scope of the claims by implicitly adding disclosed limitations which are not recited in the claims.

The claims as amended encompasses a genus of methionine repressors encoded by a genus of *metJ* genes of any nucleotide sequence and structure, a genus homoserine transsuccinylase enzymes encoded by a genus of *metA* genes, a genus S-adenosylmethionine synthetase enzymes encoded by a genus of *metK* genes, a genus cystathionine γ-synthase enzymes encoded by a genus of *metB* genes, and a genus aspartokinase-homoserine dehydrogenase II enzymes encoded by a genus of *metL* genes. The scope of each genus includes many polynucleotides with widely differing nucleotide sequences and structures, where each genus is highly variable because a significant number of structural differences between genus members exists.

The specification does not provide a nucleic acid sequence and structure common to all members of each genus of genes. There is no specific recitation of the nucleotide SEQ ID NO of

each of the recited genes in the claims. In view of the above considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Furthermore, claims 31 and 33 recite any "enhanced" activity of any homoserine transsucinylase and cystathionine γ-synthase. This encompasses a genus of any mutations that will result in the increased activity of these enzymes including altering the coding regions of the polynucleotide encoding the enzymes. However, the specification only provide a description for increasing the copy number of the polynucleotide encoding the enzymes or linking a high-expression promoter to the polynucleotide encoding the enzymes. The specification does not provide a description of any other mutations to any polynucleotide encoding any homoserine transsucinylase or cystathionine γ-synthase that results in the increase of the activity of the enzymes.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definitions, such as the structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v, Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997), quoting *Fiers v. Revel,* 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these. Therefore, the instant claims are not adequately described.

The claims are additionally rejected for the following reasons. Gene elements which are not particularly described, including regulatory elements and untranslated regions, are essential to the function of the claimed invention since the claims recite *metA, metK, metB, and metL* genes. The art indicates that the structure of genes with regulatory elements and untranslated regions is empirically determined. For example, the structural elements of "gene" mediating the expression of a particular protein in the liver may be different than the structural elements of the "gene" mediating the expression of the same protein in the brain. Therefore, the structure of these elements which applicants considers as being essential to the function of the claim are not conventional in the art.

There is no known or disclosed correlation between the coding region of a polynucleotide

encoding each of the recited methionine repressor, homoserine transsuccinylase, S-adenosylmethionine synthetase, and cystathionine γ-synthase and the structure of the non-described regulatory elements and untranslated regions of the gene.

In view of the above considerations, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of any genes encoding any methionine repressor, homoserine transsuccinylase, S-adenosylmethionine synthetase, and cystathionine γ-synthase.

6. Claims 31-33 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any type of genetic modification to the *metA* gene that will result in an enhancement of the activity of homoserine transsucinnylase or the expression regulatory sequence for the said *metA* gene; any type of genetic modification to the *metB* gene that will result in an enhancement of the activity of cystathionine γ-synthase; and any type of genetic modification to the *metL* gene that will result in an enhancement of the activity of aspartokinase-homoserine dehydrogenase II. However, the specification only provides guidance and working examples for increasing the copy number of the recited polynucleotides encoding each of the enzymes.

There are no working examples, guidance, and prediction from the specification showing how any type of genetic mutation, other than increasing the copy number of the recited polynucleotides, performed on each of the recited polynucleotides will result in the increase of activity of each of homoserine transsucinnylase, cystathionine γ-synthase, and aspartokinase-homoserine dehydrogenase II.

Thus, the amount of experimentation to make the invention is enormous and undue. Such trial and error experimentation entails screening and searching for any biological source containing any of the recited *metA, metB, and metL* genes of any nucleotide sequence, modifying

each gene at any position including any regulatory sequence(s) by any genetic modification (deleting, adding, substituting, and/or inserting nucleotide(s)), and screening for a genetic modification that will result in the increase of activity of each of the homoserine transsucinnylase, cystathionine γ-synthase, and aspartokinase-homoserine dehydrogenase II enzymes. General teaching for screening and searching for the invention is not guidance for making the claimed invention.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific nucleotide sequence of each of the *metA, metB, and metL* genes and the specific genetic mutation that will result in the increased activity of each of the encoded homoserine transsucinnylase, cystathionine γ-synthase, and aspartokinase-homoserine dehydrogenase II enzymes. Without such guidance, the amount of experimentation to make the invention is undue.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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